

CLAIMS

What is claimed is:

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1. A humanized immunoglobulin having binding specificity for $\alpha 4\beta 7$ integrin, said immunoglobulin comprising an antigen binding region of nonhuman origin and at least a portion of an immunoglobulin of human origin.
 2. The humanized immunoglobulin of Claim 1, wherein the portion of an immunoglobulin of human origin is derived from a human constant region.
 - 10 3. The humanized immunoglobulin of Claim 2 wherein the human constant region is of the gamma type.
 4. The humanized immunoglobulin of Claim 2 wherein the antigen binding region is of rodent origin.
 - 15 5. The humanized immunoglobulin of Claim 2 wherein the antigen binding region is derived from Act-1 monoclonal antibody.
 - 20 6. The humanized immunoglobulin of Claim 1 wherein the antigen binding region comprises a complementarity determining region of rodent origin, and the portion of an immunoglobulin of human origin is derived from a human framework region.
 7. The humanized immunoglobulin of Claim 6, wherein the complementarity determining region is derived from Act-1 monoclonal antibody.
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8. A humanized immunoglobulin having binding specificity for $\alpha 4\beta 7$ integrin comprising a heavy chain and a light chain,

5 the light chain comprising a complementarity determining region derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a light chain of human origin; and

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10 the heavy chain comprising a complementarity determining region derived from an antibody of nonhuman origin which binds $\alpha 4\beta 7$ and a framework region derived from a heavy chain of human origin.

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9. The humanized immunoglobulin of Claim 8 wherein said immunoglobulin can compete with murine Act-1 for binding to $\alpha 4\beta 7$.

15 10. The humanized immunoglobulin of Claim 8 wherein the light chain comprises three complementarity determining regions derived from the light chain of the Act-1 antibody, and the heavy chain comprises three complementarity determining regions derived from the heavy chain of the Act-1 antibody.

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11. The humanized immunoglobulin of Claim 8 wherein the light chain of human origin is the light chain of the GM607'CL antibody.

25 12. The humanized of Claim 8 wherein the heavy chain of human origin is the human 21/28'CL antibody.

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13. A humanized immunoglobulin light chain comprising CDR1, CDR2 and CDR3 of the light chain of murine Act-1 antibody, and a human light chain framework region.

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14. The humanized immunoglobulin light chain of Claim 13 wherein the human framework region is derived from the light chain of the GM607'CL antibody.
- 5 15. The humanized immunoglobulin light chain of Claim 14 comprising the variable region of SEQ ID NO:21.
16. An isolated nucleic acid encoding the humanized immunoglobulin light chain of Claim 15.
17. The isolated nucleic acid of Claim 16 comprising the variable region coding sequence of SEQ ID NO:20.
- 10 18. A humanized immunoglobulin heavy chain comprising CDR1, CDR2 and CDR3 of the heavy chain of the Act-1 antibody, and a human heavy chain framework region.
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- 15 19. The humanized immunoglobulin heavy chain of Claim 18 wherein the human framework region is derived from the heavy chain of the human 21/28'CL antibody.
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20. The humanized immunoglobulin heavy chain of Claim 19 comprising the variable region of SEQ ID NO:19.
21. An isolated nucleic acid encoding the humanized immunoglobulin heavy chain of Claim 20.
- 20 22. The isolated nucleic acid of Claim 21 comprising the variable region coding sequence of SEQ ID NO:18.
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23. A humanized immunoglobulin light chain, said light chain having an amino acid sequence comprising at least a functional portion of the light chain variable region amino acid sequence shown in Figure 7 (SEQ ID NO:12).

24. A humanized immunoglobulin light chain of Claim 23, said light chain having an amino acid sequence comprising the signal peptide sequence shown in Figure 7 (SEQ ID NO:12) and at least a functional portion of the light chain variable region amino acid sequence shown in Figure 7 (SEQ ID NO:12).

25. An isolated nucleic acid comprising a sequence encoding a humanized immunoglobulin light chain of Claim 23.

26. The isolated nucleic acid of Claim 25 comprising the variable region coding sequence of SEQ ID NO:11.

27. A humanized immunoglobulin heavy chain, said heavy chain having an amino acid sequence comprising at least a functional portion of the heavy chain variable region amino acid sequence shown in Figure 9 (SEQ ID NO:15).

28. A humanized immunoglobulin heavy chain of Claim 27, said heavy chain having an amino acid sequence comprising the signal peptide sequence shown in Figure 9 (SEQ ID NO:15) and at least a functional portion of the heavy chain variable region amino acid sequence shown in Figure 9 (SEQ ID NO:15).

29. An isolated nucleic acid encoding the humanized immunoglobulin heavy chain of Claim 27.

30. The isolated nucleic acid of Claim 29 comprising the variable region coding sequence of SEQ ID NO:14.

31. An expression vector comprising a fused gene encoding a humanized immunoglobulin light chain, said gene

- 5 comprising a nucleotide sequence encoding a CDR
derived from a light chain of a nonhuman antibody
having binding specificity for $\alpha 4\beta 7$ integrin and a
framework region derived from a light chain of human
origin.
32. The expression vector of Claim 31, wherein the
nonhuman antibody is murine Act-1 antibody.
33. A host cell comprising the expression vector of Claim
31.
- 10 34. An expression vector comprising a fused gene encoding
a humanized immunoglobulin heavy chain, said gene
comprising a nucleotide sequence encoding a CDR
derived from a heavy chain of a nonhuman antibody
having binding specificity for $\alpha 4\beta 7$ integrin and a
15 framework region derived from a heavy chain of human
origin.
35. The expression vector of Claim 34, wherein the
nonhuman antibody is murine Act-1 antibody.
36. A host cell comprising the expression vector of Claim
20 34.
37. A host cell comprising a first recombinant nucleic
acid encoding a humanized immunoglobulin light chain
and a second recombinant nucleic acid encoding a
humanized immunoglobulin heavy chain,
25 said first nucleic acid comprising a nucleotide
sequence encoding a CDR derived from the light chain
of murine Act-1 antibody and a framework region
derived from a light chain of human origin; and

said second nucleic acid comprising a nucleotide sequence encoding a CDR derived from the heavy chain of murine Act-1 antibody and a framework region derived from a heavy chain of human origin.

- 5 38. A method of preparing a humanized immunoglobulin comprising maintaining a host cell of Claim 37 under conditions appropriate for expression of a humanized immunoglobulin, whereby humanized immunoglobulin chains are expressed and a humanized immunoglobulin is
10 produced.
39. The method of Claim 38 further comprising the step of isolating the humanized immunoglobulin.
40. A fused gene encoding a humanized immunoglobulin light or heavy chain comprising:
15 a) a first nucleic acid sequence encoding an antigen binding region derived from murine Act-1 monoclonal antibody; and
b) a second nucleic acid sequence encoding at least a portion of a constant region of an
20 immunoglobulin of human origin.
41. A method of inhibiting the interaction of a first cell bearing $\alpha 4\beta 7$ with a second cell bearing a ligand thereof, comprising contacting said first cell with an effective amount of a humanized immunoglobulin of
25 Claim 1.
42. A method of inhibiting leukocyte infiltration of mucosal tissue, comprising administering to a patient an effective amount of a humanized immunoglobulin of Claim 1.

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43. A method of therapy of a disease associated with leukocyte infiltration of tissues expressing the molecule MAdCAM-1, comprising administering to a patient an effective amount of a humanized immunoglobulin of Claim 1.
44. The method of Claim 43, wherein the disease is a disease associated with leukocyte infiltration of tissues as a result of binding of leukocytes to gut-associated endothelium expressing the molecule MAdCAM.
- 10 45. A method for treating inflammatory bowel disease in a patient, comprising administering to the patient an effective amount of a humanized immunoglobulin of Claim 1.
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